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REGIO- AND STEREOSELECTIVE FORMATION OF 1,3-OXATHIOLANES BY REACTIONS OF THIOCARBONYL COMPOUNDS WITH OXIRANES

Changchun Fu, Milen Blagoev, Anthony Linden, and Heinz Heimgartner

*Institute of Organic Chemistry, University of Zürich
Winterthurerstrasse 190, CH-8057 Zürich, Switzerland*

E-mail: heimgart@oci.unizh.ch

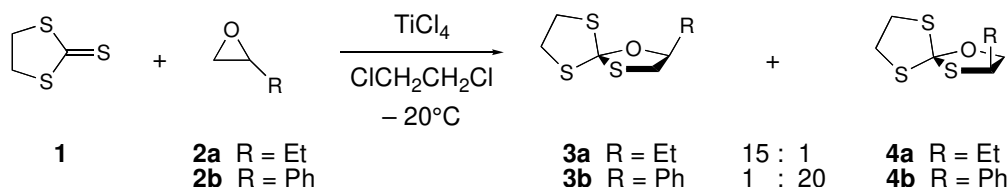
Abstract

Lewis acid-catalyzed reactions of oxiranes with a variety of C=S compounds yield 1,3-oxathiolanes. The ring enlargement of monosubstituted oxiranes occurs regioselectively via cleavage of the O,C(3) bond of alkyl substituted oxiranes and the O,C(2) bond of phenyl oxirane. Furthermore, the reaction proceeds with inversion of the configuration at the center of the nucleophilic attack by the S-atom. The formation of thiocarbonylium ions as intermediates is supported by Wagner-Meerwein type rearrangements. Enolized thioketones react with oxiranes to give enesulfanyl alcohols, which undergo an acid-catalyzed cyclization to yield 1,3-oxathiolanes.

INTRODUCTION

In general, 1,3-oxathiolanes are prepared by the reaction of carbonyl compounds with 2-sulfanylalkan-1-ols. Alternatively, 1,3-dipolar cycloadditions of carbonyl ylides with C=S and thiocarbonyl ylides with C=O compounds, respectively, lead to the same heterocyclic system (cf. refs. cited in [1]). Some years ago, we discovered that the Lewis acid-catalyzed reaction of oxiranes with 4,4-disubstituted 1,3-thiazole-5(4*H*)-thiones and trithiocarbonates, respectively, offers another convenient access to 1,3-oxathiolanes [1,2]. For example, 1,3-dithiolane-2-thione (**1**) and 2-ethyloxirane (**2a**) in 1,2-dichloroethane and TiCl₄ at –20°C gave the spirocyclic 1,3-oxathiolanes **3a** and **4a** (R = Et) in a ratio of 15:1 (Scheme 1). On the other hand, the ratio **3b**/**4b** (R = Ph) was determined to be 1:20 [2].

Scheme 1

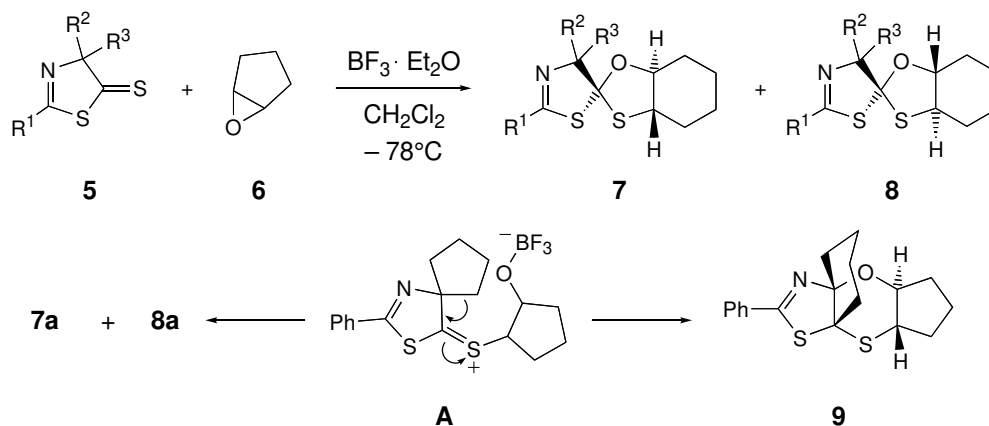


RESULTS

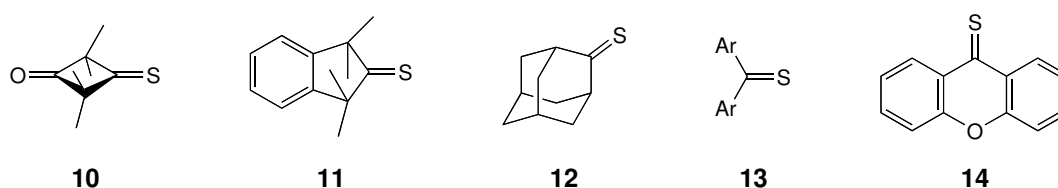
Treatment of a mixture of a 1,3-thiazole-5(4*H*)-thione **5** and 1,2-epoxycyclopentane (**6**) in dichloroethane at –78°C with BF₃·Et₂O gives the two diastereoisomeric 1,3-oxathiolanes **7** and **8** in 74–84% yield (ratio ca. 3:1) [3] (Scheme 2). Another efficient catalyst is SnCl₄. Both isomers show a *trans*-fusion of the cyclopentane and 1,3-oxathiolane ring. Analogous results are obtained with 1,2-epoxycyclohexane [3] and *cis*- and *trans*-2,3-dimethyloxirane [4]. Obviously, the opening of the oxirane ring occurs by nucleophilic attack of the S-atom under

inversion of the configuration (S_N2 -type), leading to an intermediate thiocarbonylium cation of type **A**. An indication of the cationic intermediate is the Wagner-Meerwein rearrangement, which leads to the minor product **9**.

Scheme 2

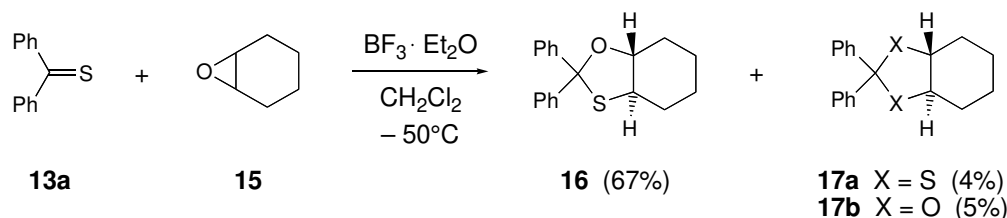


Recently, it has been shown that the reaction of 4,4-dimethyl-2-phenyl-1,3-thiazole-5(4*H*)-thione (**5a**) and (*R*)-2-phenyloxirane ((*R*)-**2b**) in dichloromethane can also be catalyzed by SiO_2 [5]. The corresponding spirocyclic 1,3-oxathiolanes are formed with high diastereoselectivity and inversion of the configuration of the oxirane. Similar results are obtained with non-enolizable thioketones such as **10** – **14** [4 – 7].



In some cases, 1,3-dithiolanes and 1,3-dioxolanes are formed in addition to 1,3-oxathiolanes [4,6,7]. For example, the BF_3 -catalyzed reaction of thiobenzophenone (**13a**) and 1,2-epoxycyclohexane (**15**) in dichloromethane at -50°C yields **16**, **17a**, and **17b** [6]. It has been shown that **17a** and **17b** are secondary products, which are formed by decomposition of **16** to give benzophenone and 1,2-epithiocyclohexane and subsequent reaction with oxirane **15** and thiobenzophenone **13a**, respectively.

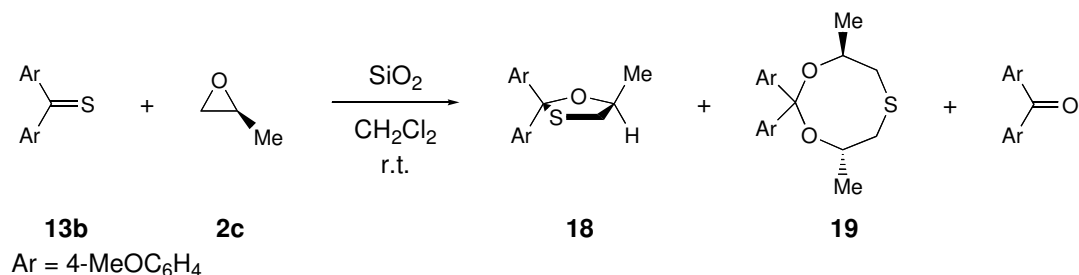
Scheme 3



Another minor product, observed in the reaction of 4,4'-dimethoxythiobenzophenone (**13b**) with 2-methyloxirane (**2c**) is the 1,3,6-dioxathiocane **19** [7,8] (Scheme 4). It is noteworthy that only the homochiral *trans* isomer is formed even though racemic **2c** is used. The same product is obtained when a mixture of the major product **18** and **2c** is treated with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ at

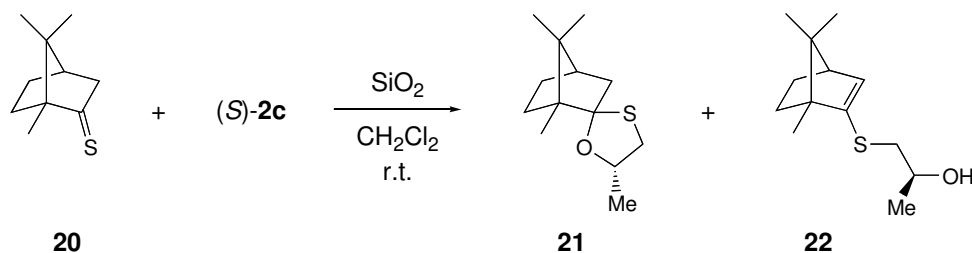
–90°C. Using (*S*)-**2c** in the reaction with **13b**, (*S*)-**18** and (*S,S*)-**19** are formed with 98 and >99% ee, respectively. On the other hand, no 1:2 adduct (*R,S*)-**19** could be detected in attempted reactions of (*R*)-**18** with (*S*)-**2c**.

Scheme 4



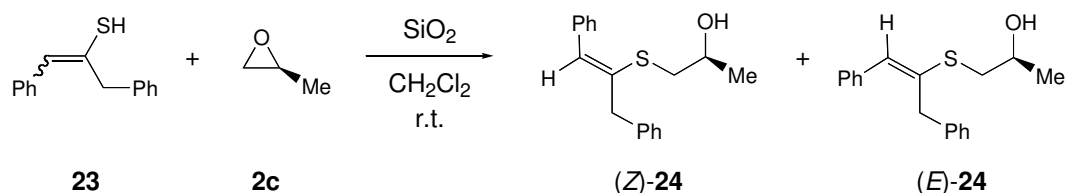
In the case of enolizable thiocamphor (**20**), the SiO₂-catalyzed reaction with (*S*)-**2c** leads to a mixture of the 1,3-oxathiolane **21** and the enesulfanyl alcohol **22** [9] (Scheme 5). The latter can be cyclized under acidic conditions to give a mixture of **21** and a diastereoisomer. The 1,3-oxathiolane **21** is acid-sensitive and undergoes a rearrangement to the second diastereoisomer. This isomerization shows clearly that the formation of the 1,3-oxathiolanes is reversible.

Scheme 5



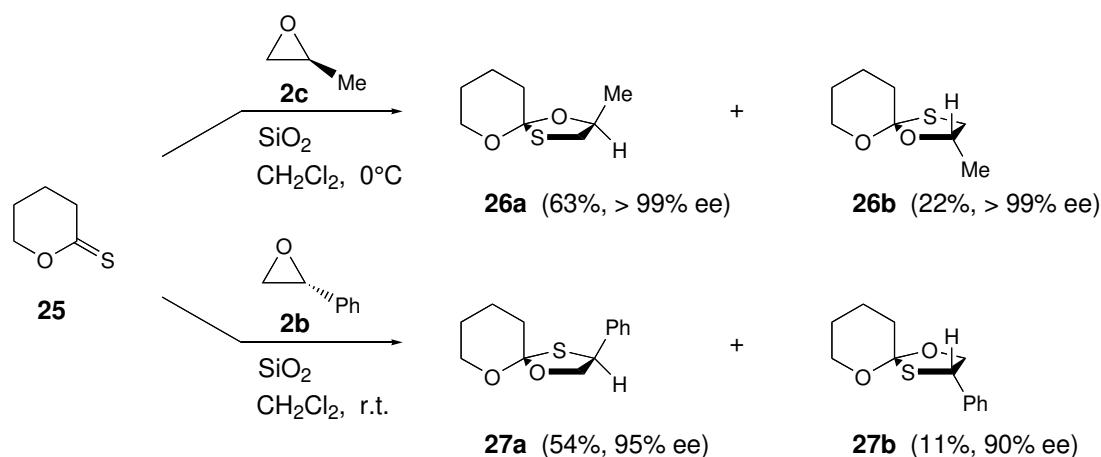
With 1,3-diphenylprop-1-ene-2-thiol (**23**), the enolized form of dibenzylthio ketone, 2-methyl- and 2-phenyloxirane react under SiO₂ catalysis to give *E/Z* isomers of the corresponding enesulfanyl alcohols with high ee values [8] (Scheme 6). On treatment with HCl gas, a cyclization to yield 1,3-oxathiolanes takes place.

Scheme 6



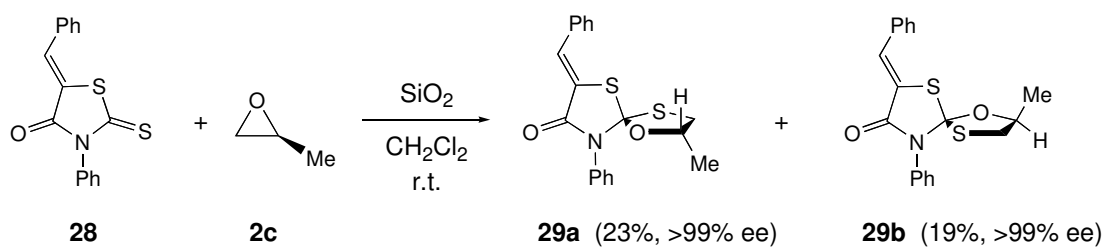
Similar to thioketones, thiolactones react with **2b** and **2c**. For example, the SiO₂-catalyzed reaction of **25** leads to spirocyclic O,O,S-orthoesters **26** and **27**, respectively, with high stereoselectivity [10] (Scheme 7).

Scheme 7



Furthermore, chemo-, regio- and stereoselective 1,3-oxathiolane formations are observed with (Z)-5-benzylidene-3-phenyl-2-thioxo-1,3-thiazolidin-4-one **28** [11] (Scheme 8). With (S)-2-methyloxirane ((S)-**2c**), after 50% conversion of **28**, the 1,3-oxathiolanes **29a** and **29b** are obtained in 23 and 19% yield, respectively.

Scheme 8



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